A mark-up copy of the amendments to the claims is attached hereto as **Exhibit A.**

REMARKS

Claims 1-47 are pending in the subject application with claims 1-14 and 29-47 withdrawn from consideration. Applicants have hereinabove canceled claims 1-20, 23, 24, 25, and 28-47, amended claims 21, 22, 26, and 27, and added new claims 48 to 51. Applicants maintain that the amendments to the claims raise no issue of new matter. Support for amended claim 21 can be found in the specification as originally filed, *inter alia*, at page 38, lines 1-12. Support for amended claim 22 can be found in the specification as originally filed, *inter alia*, at page 38, lines 26-29. Claim 26 has merely been amended to correct dependency. Support for amended claim 27 can be found in the specification as originally filed, *inter alia*, at page 39, lines 13-14. Support for new claim 48 can be found in the specification as originally filed, *inter alia*, at page 37, lines 1-13; at page 9, lines 3-5; page 37, lines 15-17; and page 10 lines 3-30. Support for new claim 49 can be found in the specification, *inter alia*, at page 10, lines 25-26. Support for new claim 50 can be found in the specification as originally filed, *inter alia*, at page 39, line 21, to page 41, line 2. Support for new claim 51 can be found in the specification as originally filed, *inter alia*, at page 39, line 14. Accordingly, applicants respectfully request entry of this Amendment. Upon entry of this Amendment claims 21, 22, 26, 27, and 48 to 51 will be pending and under examination.

In the May 21, 2002 Office Action, the Examiner stated that applicants' election with traverse of Group IV (claims 15-28) in Paper No. 9, filed: 04 June 2001, is acknowledged and that the traversal is on the ground(s) that the groups are not independent

and distinct, and have no burden of search. The Examiner stated the argument is found non-persuasive because the groups are distinct and the burden of search was established in the Office Action mailed 08 May 2001. The Examiner stated that applicant elected a species with traverse for Group IV in Paper No. 11, filed October 5, 2001. The Examiner stated that the species restriction of SEQ ID NO: 1 is acknowledged, and that because applicant did not distinctly and specifically point out the supposed errors in the species election, the election has been treated as an election without traverse (MPEP §818.03(a)). The Examiner stated that the requirement is still deemed proper and is therefore made FINAL. The Examiner stated claims 1-47 are pending, with claims 1-14 and 29-47 are withdrawn from further consideration pursuant to 37 CFR 1.142(b), as being drawn to a nonelected invention, there being no allowable generic or linking claim. The Examiner stated that applicant timely traversed the restriction (election) requirement in Paper No.'s 9 and 11.

Drawings

The Examiner stated that applicant is hereby notified that the required timing for the correction of drawings has changed, see the last 6 lines on the sheet which is attached to the back of the PTO-948, entitled "Attachment for PTO-948 (Rev. 03/01 or earlier)". The Examiner stated that due to the above notification Applicant is required to submit drawing corrections within the time period set for responding to this Office Action, failure to respond to this requirement may result in abandonment of the instant application or a notice of a failure to fully respond to this Office Action.

In response, applicants attach hereto as **Exhibit C** new corrected

drawings in compliance with PTO-948.

Claims Rejected Under 37 C.F.R. §112 - First Paragraph

The Examiner stated that claims 15-28 are rejected under 35 U.S.C. §112, first paragraph, as containing subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention. The Examiner stated that the factors to be considered in determining whether a disclosure would require undue experimentation have been summarized in *Ex parte Forman*, 230 USPQ 546 (BPA 1986) and reiterated by the Court of Appeals in *In re Wands*, 8 USPQ2d 1400 at 1404 (CAFC 1988). The Examiner stated that the factors to be considered in determining whether undue experimentation is required include: (1) the quantity of experimentation necessary, (2) the amount or direction presented, (3) the presence or absence of working examples, (4) the nature of the invention, (5) the state of the prior art, (6) the relative skill of those in the art, (7) the predictability or unpredictability of the art, and (8) the breadth of the claims. The Examiner stated that the board also stated that although the level of skill in molecular biology is high, the results of experiments in genetic engineering are unpredictable. The Examiner stated that while all of these factors are considered, a sufficient amount for a prima facie case are discussed below.

The Examiner stated that the instant application fails to provide guidance to one of ordinary skill in the art for designing a compound that binds to the stem cell factor (SCF) receptor. The Examiner stated that the specification in figure 6B discloses a representational structure of the receptor, yet the description

utilizes various colors to describe particular regions that are not visible in the black and white prints that are part of the application. The Examiner stated that in addition, even if the color was visible and the regions notable, the structure would not be reproducible. The Examiner stated that specification does not provide or suggest the crystal structure of the SCF receptor that is reproducible to enable one of ordinary skill in the art to know how to design a compound by the steps described that will bind to its binding site. The Examiner stated that the specification lacks guidance in the generation of the structure, the examples provided are a description of the SCF and methods of mimicking the SCF structure in order to potentially bind to the SCF receptor. The Examiner stated that none of the examples provide a description of the SCF receptor, the design method claimed relies upon the three-dimensional structure of the SCF and not the SCF receptor. The Examiner also stated that determining compounds that bind to the SCF have no indication of whether or not they will bind to the SCF receptor. The Examiner stated that while working examples are not, per se, required, the specification must provide adequate guidance such that one of skill in the art could practice the invention without undue experimentation. The Examiner further stated that given the lack of descriptive working examples in the specification, and the unpredictability of designing receptor binding compounds, the specification, as filed is not enabling for the method of designing a compound capable of binding to the receptor site of the SCF receptor as claimed.

The Examiner stated that, in addition, the specification fails to provide guidance to one of ordinary skill in the art to generate each and every crystal structure for the "portion/fragment" (line 7) of the SCF polypeptide. The Examiner

stated that the specification does not provide or suggest the resolutions of each and every possible crystal structure to enable one ordinary skill in the art to know how to reproduce these portion or fragment structures. The Examiner also stated that none of the examples provide a description as to the generation of these crystals, and while working examples are not, per se, required the specification must provide adequate guidance such that one of skill in the art could practice the invention without undue experimentation. The Examiner further stated that given the lack of descriptive working examples in the specification, and the unpredictability of crystallography, the specification, as filed is not enabling for using each and every crystal structure of the portion/fragment of the SCF polypeptide as claimed.

In response, without conceding the correctness of the Examiner's position and in order to expedite prosecution, applicants have canceled claim 15 and added new claim 48. Applicants note that new claim 48 is directed to a method of designing a compound capable of binding to the SCF-binding site on the Kit, based on the 3-D structure of the Kit-binding site on SCF. Applicants note that claim 48 makes it clear that the 3-D crystal structure mentioned is that of a Kit-binding site on SCF, and not of the Kit itself. Further, although the Examiner states that "determining compounds that bind to the SCF have no indication of whether or not they will bind the SCF receptor", applicants note that in the specific case of determining the structure of a Kit-binding site on a SCF, such information will in fact indicate if a designed compound will bind to the Kit. As such, applicants note that there is no need to generate the structure of the Kit as stated by the Examiner. In addition, the specification as originally filed provides working examples of

such compounds designed based on the X-ray crystallographic structure of SCF e.g. see pages 77 to 78.

With regard to claim 48, applicants note that the specification provides adequate guidance to one of ordinary skill in the art to generate crystal structures for SCF portions in the clear explication of generating the crystal structure of SCF given, for example at page 48, line 9 to page 49, line 21 and page 57, lines 3 - 21.

In addition, applicants note that although some experimentation would be required this would not amount to undue experimentation, that the specification provides guidance as exemplified above, that working examples of the compounds designed by the method are detailed in the specification (for example see pages 77 to 78), and that those in the art have a high level of skill, and that, X-ray crystallography is routine, uses extensive automation, and has been an established field for more than 50 years.

Claims Rejected Under 37 C.F.R. §112 - Second Paragraph

The Examiner stated that claims 15-28 are rejected under 35 U.S.C. §112, second paragraph, as being indefinite for failing to particulary point out and distinctly claim the subject matter which applicant regards as the invention.

The Examiner stated that claim 15 lacks clarity in the claim language "stem cell factor (SCF) receptor site" in line 2. The Examiner stated that it is unclear if the receptor site indicates the receptor site of the receptor itself or the receptor site of the stem cell factor. The Examiner stated that as such claims 16-28 which are dependent from claim 15 are also unclear.

The Examiner stated that claim 15 is unclear as to the goal of the method of designing a compound. The Examiner stated that the body of the method claim has confusing steps as to what is intended to be designed: a compound that binds to the SCF itself in its receptor site binding region; or a compound that binds to the SCF receptor as recited in line 13 of step b. The Examiner also stated that as such claims 16-28 which are dependent from claim 15 are also unclear.

The Examiner stated that claim 15 lacks clarity in the claim language concerning the atomic coordinate (lines 7-8) limitations of the claim. The Examiner stated that it is unclear if the three dimensional SCF structure is limited to the particular crystal atomic coordinates disclosed within the specification; if not, then none of the other crystal structures at their different resolutions are supported by the specification, but the crystal structure of SCF disclosed.

The Examiner stated that claim 15 lacks clarity due to the use of the term "entity" in line 12. The Examiner stated that metes and bounds of that which defines "entity" are unclear.

In response, without conceding the correctness of the Examiner's position and in order to expedite prosecution, applicants have canceled claim 15 and added new claim 48 to more particularly point out and distinctly claim the subject matter. Specifically, the claims have been amended to recite the term "Kit" instead of "SCF-receptor" in order to clarify what the intended goal of the method is and which site is meant. Applicants note that the term "entity" does not appear in new claim 48.

The Examiner stated that claim 17 and 18 are unclear as to which

part of Figure 6, 7A or 7B are being referred to. The Examiner stated that it is unclear because the figures are described per color coded regions, yet the figures of the instant application are in black and white.

The Examiner stated that claim 19 refers to Figure 10B which recites the limitations F_1, F_2, F_3, etc. The Examiner stated that there is no antecedent basis for these limitations in the claim.

The Examiner stated that the term "present" of claim 24 is a relative term the renders the claim indefinite. The metes and bounds of that which defines "present" are unclear.

The Examiner stated that claim 25 recites the limitation "the linker" in line 1, there is no antecedent basis for this limitation in the claim.

The Examiner stated that claim 25 and 28 recite the limitation "the conjugation moiety" in lines 4-5, there is no antecedent basis for this limitation in the claim.

The Examiner stated that claims 17-20 are objected to due to the improper incorporation of figures by reference in the claims.

In response, without conceding the correctness of the Examiner's position and in order to expedite prosecution, applicants have canceled claims 17, 18, 19, 20, 23, 24, 25, and 28 without disclaimer or prejudice, and amended claims 21, 22, 26, and 27. The claims, as amended, and new claims 50 and 51, do not incorporate figures by reference, have antecedent basis for terms recited, and more particulary point out and distinctly claim the subject matter.

Mark-Up Copy of Amendments to Claims

Claims 15, 21, 22, 26, 27 have been amended as follows:

--21. (Amended) The method of claim [20] 50, wherein [the ooligopeptide comprises a sequence, wherein functional moiety] F_1 corresponds to a segment of amino acid residues from within N-terminal residues 1-10 of SCF (SEQ ID NO:1), [functional moiety] F_2 corresponds to a segment of amino acid residues from within residues 79-95 of SCF, and [functional moiety] F_3 corresponds to a segment of amino acid residues located within three amino acid residues of amino acid residue 127, and where, in [wherein F_1, F_2, and F_3 are connected by connecting peptide segements] X_n, X_m, and X_p[,] respectively, [wherein] n=0-5, m=0-5 and p=3-8 amino acid residues[, respectively, and the conjugation moiety F_L is a cysteine residue].--

--22. (Amended) The method of claim [21] 50, wherein [the functional moieties] F_1, F_2, and F_3 [on the ligand heads] have been selected by bacterial phage display for optimal receptor binding.--

--26. (Amended) The method of claim [25] 50, wherein the organic polymer is polyethyleneglycol (PEG) comprising the structure $H[OCH_2CH_2]_nOH$, wherein n is 10-20.--

--27. (Amended) The method of claim [25] 50, wherein the capping moiety[, F_c,] is a thiol-reactive group [such as N-ethyl maleimide].